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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,979	02/22/2002	Phillip Dan Cook	ISIS-5028	9967
34138	7590	01/04/2006	EXAMINER	
COZEN O'CONNOR, P.C. 1900 MARKET STREET PHILADELPHIA, PA 19103-3508			BOWMAN, AMY HUDSON	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/080,979	Applicant(s) COOK ET AL.	
	Examiner Amy H. Bowman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12 and 14-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12 and 14-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/2/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 12/2/2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 8/9/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-11, 13 and 17-22 have been cancelled. Claims 12 and 14-16 are pending in the application.

Response to Arguments--Claim Rejections - 35 USC § 102(a) or (e)

Claims 12 and 14-16 stand rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Dean et al. (US 6,312,900 B1), for the reasons of record set forth in the office action mailed 8/9/2005 and reiterated herein. Applicant has cancelled claims 1, 3-7, 9 and 10, obviating the rejection against these claims.

Applicant asserts that Dean et al. does not teach a method of treatment of a hepatic disease by administration of an oligonucleotide having at least two sterol moieties covalently bonded thereto. Applicant argues that Dean et al. teaches that lipophilic moieties can be attached to oligonucleotides to enhance cellular uptake, but does not teach enhanced uptake to the liver.

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Contrary to applicant's assertions, Dean et al. is considered to teach each of the required elements of the instant claims. Dean et al. teach a method of inhibiting expression of a nucleic acid comprising contacting cells or tissues with an antisense oligonucleotide, wherein the oligonucleotide comprises at least one lipophilic moiety, more specifically cholesteryl moieties, which enhances the cellular uptake of said antisense oligonucleotide (see claims 1, 2 and 27). The teaching of at least one cholesteryl moiety meets the instant limitation of two sterol moieties. Dean et al. teach that the oligonucleotides of the invention are contacted with animal cells either *in vivo* or *ex vivo* (see column 11) and specifically teach targeting nucleic acids in adult mice *in vivo* and resultant treatment of tumor growth (see example 4). Dean et al. teach that the lipophilic moieties may be linked to the oligonucleotide at several different positions on the oligonucleotide, including the 3', 5' or 2' positions (see column 9). Additionally, Dean et al. teach that the oligonucleotides can be delivered to the liver (see column 15). Dean et al. teach delivery via colloidal dispersion systems, wherein liposomes naturally distribute to cells of the reticuloendothelial system (see column 16). Although Dean et al. do not specifically exemplify delivering an oligonucleotide specifically to the liver, Dean et al. specifically teach that the oligonucleotides of the invention can be delivered to the liver. The oligonucleotides taught by Dean et al. are taught for the purpose of treating and diagnosing diseases or disorders (see abstract, for example). If the oligonucleotides are being specifically delivered to the liver, the oligonucleotides would necessarily be utilized to treat a disease or disorder associated with the liver. Applicant argues that Dean et al. teach the treatment of a subcutaneous tumor rather than a

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hepatic disease or disorder. Dean et al. exemplify in vivo treatment of a subcutaneous tumor and further teach that oligonucleotides of the invention can be targeted to the liver, which would necessarily be delivered to the liver for pharmaceutical purposes. It is noted that the instant specification teaches oligonucleotide delivery to the liver, but does not exemplify treatment of a hepatic disease or disorder as a result of targeting such oligonucleotides to the liver. Therefore, both the instant specification and Dean et al. are considered to teach the required structural elements of the instant claims, rather than to exemplify the intended use of the preamble. Since both specifications have similar teachings, both are considered similarly enabled. If the invention is claimed, it is presumed to be enabled.

In the instant case, the terminology of the preamble reciting "a method of treating a mammal having a hepatic disease or disorder" is not considered to limit the structure of the claimed invention. If the body of the claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed inventions limitations, then the preamble is not considered a limitation and is of no significance to the claim construction. The recited purpose or intended use must result in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art (see MPEP 2111.02).

In the instant case, Dean et al. teach each of the required method steps, administering an antisense oligonucleotide to a mammal and that the oligonucleotides of the invention can be linked to the oligonucleotide at several different positions on the

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oligonucleotide, including the 3', 5' or 2' positions. Dean et al. specifically teach that the oligonucleotides of the invention can be targeted to the liver and would necessarily be utilized for therapeutic purposes related to the liver. Applicant argues that Dean et al. does not teach enhanced hepatic uptake, although this is not a limitation of the instant claims. Dean et al. teaches each of the active method steps, as explained above, and would necessarily result in enhanced hepatic uptake. Applicant argues that Dean et al. teaches that a hepatic catheter can be used to deliver the oligonucleotide to the liver, as well as colloidal dispersion systems, but does not teach covalent bondage of lipophilic groups to oligonucleotides. Although applicant's assertions support that Dean et al. teach methods of specifically targeting the liver with oligonucleotides modified with cholesteryl, the examiner has not relied on such teachings for covalent bondage. Dean et al. teach that the lipophilic moieties may be linked to the oligonucleotide at several different positions on the oligonucleotide, including the 3', 5' or 2' positions (see column 9), which is identical to the instant claim limitations.

Conclusion

All claims are drawn to the same invention claimed in the earlier prosecution of the instant application and are finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.


Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

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5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Amy H. Bowman
Examiner
Art Unit 1635


J.D. SCHULTZ, Ph.D.
PATENT EXAMINER